AD_____

AWARD NUMBER:
W81XWH-12-1-0607

TITLE:
Emotion Regulation Training for Treating Warfighters with Combat-Related PTSD Using Real-Time fMRI and EEG-Assisted Neurofeedback.

PRINCIPAL INVESTIGATOR:
Jerzy Bodurka

.NSTITUTION :
Laureate Institute for Brain Research
Tulsa, OK 74137

REPORT DATE:
September 2013

TYPE OF REPORT:
Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release; Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE	**2. REPORT TYPE**	**3. DATES COVERED**
September 2013	Annual	30September2012–29September2013

4. TITLE AND SUBTITLE
Emotion Regulation Training for Treating Warfighters with Combat-Related PTSD Using Real-Time fMRI and EEG-Assisted Neurofeedback.

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-12-1-0607

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Jerzy Bodurka
E-Mail: jbodurka@laureateinstitute.org

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Laureate Institute for Brain Research
Tulsa, OK 74137

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
PTSD is a chronic and disabling condition characterized by dysregulated fear, anxiety, anger, and depression. Neurocircuitry-based models of PTSD emphasize dysregulation of the amygdala, which is involved in the regulation of PTSD-relevant emotions. We are utilizing real-time functional magnetic resonance imaging neurofeedback (rtfMRI-nf) training with concurrent electroencephalography (EEG) recordings to directly target and modulate the emotion regulation neurocircuit. By using the multimodal data, we can determine which EEG signals/leads or their combination specifically predict or correlate with clinical improvement associated with the rtfMRI-nf training. During year 1 we have secured IRB approval and a Certificate of Confidentiality for the project and are actively enrolling veterans to complete rtfMRI-nf neurofeedback training with simultaneous EEG recordings, and a pre-, post-training clinical assessment battery to evaluate improvement on the psychological and behavioral domains affected in combat-related PTSD (Aim1). Our extensive recruitment campaign is currently yielding several potential participant contacts per week, resulting in ongoing Veteran enrollment in the project at a rate consistent with our goals during this phase of the project. We also have begun developing the software/hardware system for a stand-alone EEG training paradigm as proposed (Aim2).

15. SUBJECT TERMS
PTSD; amygdala; fMRI; EEG; real-time fMRI neurofeedback; simultaneous EEG-fMRI; emotion regulation

16. SECURITY CLASSIFICATION OF:	**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES 13**	**19a. NAME OF RESPONSIBLE PERSON** USAMRMC pages		
a. REPORT U	**b. ABSTRACT** U	**c. THIS PAGE** U	UU	21	**19b. TELEPHONE NUMBER**

Table of Contents

1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Post-traumatic stress disorder (PTSD) is a chronic and disabling psychiatric condition. Individuals with PTSD suffer from the dysregulation of several types of emotion, including fear, anxiety, anger, and depression [1–4]. Neurocircuit models of PTSD emphasize the role of the amygdala and its reciprocal interactions with the ventromedial prefrontal cortex (vmPFC) [5–9]. To advance understanding of the treatment of combat-related PTSD, the current state-of-the-art research aims to test ways to modulate the functions of the emotion circuit implicated in PTSD. We utilize the recent advances in real-time functional magnetic resonance imaging neurofeedback (rtfMRI-nf) to directly target and modulate amygdala activity [10–11]. This technique measures neuronal activity with sufficiently high temporal resolution that information from the amygdala is immediately available to form a feedback loop. In parallel with rtfMRI-nf, we will obtain simultaneous measurement of electroencephalography (EEG) signals, which directly reflect brain activity in the cerebral cortex [12]. By using the multimodal imaging data we can determine which EEG signals/leads or their combination specifically predict or correlate with clinical improvement that has been associated with the rtfMRI-nf training [11,13–16]. This knowledge will enable us to establish a translational path toward the development of stand-alone real-time EEG neurofeedback (rtEEG-nf) training for emotion regulation, which can facilitate the widespread implementation of the treatment approach due to the high portability and relatively low cost of EEG systems. Our *main objective* is to determine whether rtfMRI- and rtEEG-assisted neurofeedback emotion regulation training protocols can reduce the symptoms of combat-related PTSD.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

   Combat-related PTSD, fMRI, EEG, emotions, amygdala, neurofeedback

3. **OVERALL PROJECT SUMMARY:** Summarize the progress during appropriate reporting period (single annual or comprehensive final). This section of the report shall be in direct alignment with respect to each task outlined in the approved SOW in a summary of Current Objectives, and a summary of Results, Progress and Accomplishments with Discussion. Key methodology used during the reporting period, including a description of any changes to originally proposed methods, shall be summarized. Data supporting research conclusions, in the form of figures and/or tables, shall be embedded in the text, appended, or referenced to appended manuscripts. Actual or anticipated problems or delays and actions or plans to resolve them shall be included. Additionally, any changes in approach and reasons for these changes shall be reported. **Any change that is substantially different from the original approved SOW (e.g., new or modified tasks, objectives, experiments, etc.) requires review by the Grants Officer's Representative and final approval by USAMRAA Grants Officer through an award modification prior to initiating any changes.**

Overall, during the first year of the project period we have finalized the study protocol, secured all necessary approvals to begin the study, initiated a large recruitment campaign, and are actively enrolling participants into the study at a rate that will allow us to achieve our main aims in a timeframe comparable to that proposed. What follows is a detailed chronological account of these activities.

In the first 4 months of the project we successfully completed all study preparation and initiation necessary to conduct the funded research at the Laureate Institute for Brain Research (LIBR). These activities included securing IRB approval and obtaining a certificate of confidentiality. After securing human subjects research approval from the Department of Defense Human Research Protection Office (DoD HRPO) on 2/19/13, participant recruitment was initiated on 2/23/13. As a supplement to regular communications among study investigators via email, phone meetings, video conferences, etc., we have also established regular weekly progress report meetings where we discuss current project needs, problems, and relevant activities with all investigators, including co-investigators Drs. Feldner (University of Arkansas) and Krueger (George Mason University), both joining via video or teleconference. Technical and logistic preparations also have been completed including: i) multiple software improvements and enhancements for robustness and speed of the rtfMRI system; ii) modified EEG and fMRI data acquisition, in particular better synchronization between our MRI scanner and EEG amplifier to further improve MRI artifact corrections in EEG data simultaneously acquired with fMRI; iii)

developing and programming fMRI pre/post emotional counting Stroop tasks and computer-based questionnaires; iv) creating a dedicated phone screening for the study; v) staff training for interview and PTSD assessments; and vi) subject visit logistics planned and established (including scheduling for assessments, MRI scans, and clinical coverage).

In summary we have accomplished the following outcomes as proposed in the originally submitted statement of work:

1.1.a Programming: fMRI pre/post tasks and computer-based subject questionnaires were completed by the Laureate Institute for Brain Research (LIBR) staff as proposed during the first two months of the project.

1.1.b. Training of staff at LIBR for PTSD assessment was completed with LIBR and University of Arkansas (UA) staff as proposed during the second month of the project.

Project Milestone #1 Human subject use approval: This milestone was met during the first year of the project. Approval from Western Institutional Review Board was secured 11/9/2012. USAMRMC ORP HRPO approval was obtained 2/19/2013. In addition, a Certificate of Confidentiality was obtained on 11/21/2012.

1.1.c Recruitment, screening, and assessment were begun and have been ongoing at the LIBR during months 5 through 12 of year 1.

1.1.d fMRI/EEG: Study procedures have been completed with 3 subjects between months 5 and 12 during the first year at the LIBR. Another 5 subjects have been enrolled and are completing study procedures.

1.1.e fMRI/EEG, psychological tests: Data analysis has been ongoing as subjects complete study procedures to ensure data quality and subject safety. Although too few subjects have completed the protocol to draw inferences at this stage, data quality is high and no adverse events have arisen with respect to subject safety.

1.1.f We have begun EEG software development at the LIBR during month 12 of the project.

We also are currently collecting rtfMRI-nf and EEG data for this study, aiming to reach 24 subjects for our Milestone #2, towards goals of Aim #1: establish rtfMRI-nf training feasibility with concurrent EEG recordings in a combat-related PTSD population (Phase 1, months 1–18).

Recruitment efforts description:

In October 2012, we began implementing our planned recruitment strategy with Madhu Koduri, our collaborator at the Jack C. Montgomery Veterans Administration (VA) Medical Center. Our initial plans included a combination of both passive and active recruitment strategies through the VA centers in the Tulsa area. For passive recruitment we planned to leave fliers and pamphlets in the public areas of VA buildings, post advertisements via electronic billboards in VA facilities, and provide study information that psychiatrists and other VA employees could distribute to veterans receiving care from the VA. Active recruitment would involve adding the VA Center as a research site, Dr. Koduri would serve as site PI and would need a research coordinator for IRB and VA Research and Development compliance issues. Our collaborators employed by the VA would search for possible candidates in the VA medical records.

Upon further investigation we found that an active recruitment strategy was not feasible due to VA regulations regarding using government employee time for non-VA research and Dr. Koduri's limited time availability, but we continued to pursue the avenue of passive recruitment. To begin such a strategy, in November we submitted our recruitment plan to the VA's Institutional Review Board (IRB) of record, the University of Oklahoma IRB, and the VA Research and Development Board for a determination on whether our plan for passive recruitment constituted research. We received a determination that this plan did not constitute research from the Oklahoma University (OU) IRB in January and from the VA Research and Development Board in February. We began distributing the approved recruitment materials, but in June we were informed of a new VA policy that prevented us from posting recruitment materials for non-VA studies within the premises of a VA facility. The policy did specify that

VA clinicians were allowed to provide information about a study to patients, and we continue to seek contacts at the VA who are willing to collaborate with us using this recruitment effort.

Despite these efforts, VA referrals have remained limited, and thus we have worked to expand our recruitment strategies to other sources of veterans in the community.

Since obtaining approval to begin recruitment in February, 2013, our most effective recruitment efforts have included utilizing specific media outlets to introduce our study and provide information to the veteran population about research initiatives and needs. Media resources that have been utilized include 9 advertisements on 6 different local radio stations, Facebook, Craigslist, commercial slots in Tulsa movie theaters, and local newspaper ads.

On March 19, 2013, we engaged the Community Service Council (CSC) regarding the current PTSD research. This effort yielded contacts with Carla Tanner and Jim Lyall who host monthly Veterans' Initiative meetings for veteran service providers. Beginning in the following month (April 11, 2013), recruitment efforts included attending the initiative meetings monthly, for a total of 6 (April-September) meetings sponsored by the local Veterans Initiative Council. Each month, meetings were comprised of 20-30 local and federal veteran service providers and groups. In keeping with recruitment initiatives, we constructed packets of pamphlets and brochures reviewed them with service providers during these monthly meetings, highlighting recruitment needs and the significance of research.

Recruitment efforts were also expanded to the Mental Health Association, Tulsa (MHAT). On April 12, 2013, our recruitment-focused project staff attended and presented at an event called "Crisis: Opportunity for Change." In addition to making a presentation on our research project, during the various presentations by other mental health service providers, a recruitment and information dissemination table was manned by our recruitment-focused staff and study pamphlets were handed out throughout the duration of the event; approximately 50 pieces of literature were provided to service providers. Recruitment efforts also extended to local law enforcement and attorneys. On April 18, 2013, our staff met with the Tulsa Police Department and presented information on our target population and provided a box of approximately 50

pamphlets for distribution to veteran law enforcement officers. Later the same day, an attorney from Legal Aid Services of Oklahoma was provided a packet of 75 fliers for the study that she could distribute to her veteran-status clients. On April 22, 2013, recruitment for the current study extended to media outlets; an interview with project staff was aired on KWGS, the local public radio station, to provide exposure and information to the public about the study, its current recruitment needs, and ways in which to contact our institute for participation.

Beginning on May 1, 2013, our recruitment efforts yielded a new relationship with Brookhaven Psychiatric Hospital. Each month our recruitment-focused staff attended meetings and provided approximately 235 pieces of study-focused literature to various social workers, mental health counselors, psychologists, and physicians. These recruitment efforts also included meetings and presentations with one particular selected clinician, since he works directly with the target population. Brochures have been replenished monthly or as needed. Further efforts were made in regard to specifically accessing unmedicated veterans, as this is an inclusion criterion for our study. On May 7, 2013, a meeting was held with psychotherapist Daniel Morris of Human Skills and Resources. After discussing information about the current research and requesting referrals, approximately 100 brochures were provided for clinicians and clients. Recruitment efforts were also extended to psychiatrists at the Laureate Psychiatric Clinic and Hospital (LPCH). On May 21, 2013, we hosted our first recruitment-oriented luncheon for the psychiatrists and physicians of LPCH. A display table was set up with study brochures along with a sign-in sheet for those that requested further information or had a referral at that time. These luncheons continued through September. In hopes of encouraging further interagency interaction, action was taken on May 28, 2013, to engage Family and Children Services; introductory conversations were made and pamphlets mailed for distribution to clients.

In order to engage veterans more directly, in June of 2013, recruitment-focused staff participated in the US Army National Guard's 30 Day Yellow Ribbon Event in Jenks, Oklahoma. A display table was set up and manned for the duration of the event. Primary recruitment activities involved welcoming veterans and discussing the current research project as well as providing information materials to potential participants and their loved ones. Approximately 100 packets of information were distributed.

Also, during the same month, recruitment efforts aimed to engage the larger community in learning about our research study during the Tulsa Tough athletic event. Information was distributed via our display table; questions about the research were answered, and interested parties signed up to be contacted for participation.

During the month of July, we sought to continue to engage new community organizations in partnership with our institute. Each month thereafter, fliers and pamphlets were distributed to gyms, Physical Therapy of Tulsa, Neurosurgery Associates, and ear/nose/throat specialists. With permission, our staff placed study brochures on multiple tables in the lobby areas and provided information to staff. On July 13-14, 2013, our recruitment staff attended the 60 Day Yellow Ribbon Event held by the US Army National Guard in Tulsa. As in the prior month, a display table was set up and manned for the duration of the event; primary activities involved welcoming veterans and discussing our research project as well as providing informational materials to potential participants and their loved ones. Approximately 130 packets of information were distributed. Also, on July 21, 2013, Muskogee VA held its Welcome Home event at the (Bank of Oklahoma) BOK Center in downtown Tulsa and recruitment staff set up two display tables and dispersed information as well as key chains and cell phone holders with our institute's logo to serve as a reminder of the PTSD research being conducted.

In the month on August 2013, recruitment efforts included providing a tour of our institute to the News on 6 crew. Dr. Bodurka provided a presentation of our research study and recruitment needs. Our interview and presentation aired on KOTV on August 22, 2013 during the 5:00pm and 10:00pm time slots. On August 27, 2013, we welcomed the Attorney General and formally presented information about our research study and our goals.

In September, 2013, recruitment staff attended the Soul Wounds veterans' ceremony at All Souls Unitarian Church in Tulsa. With permission, our staff placed study brochures on tables in the lobby areas and provided information to attendees. On September 19, 2013, recruitment forged a new partnership with the Veteran Advisory Council and presented information about our research study, target population and recruitment needs; pamphlets were distributed to

approximately 43 community veteran service providers. Recruitment-focused staff presented before The University of Tulsa Student Veteran Association; after the presentation, staff remained and answered questions about our research study and left brochures for attendees. On September 26, 2013, recruitment staff attended a meeting at a local (Veterans of Foreign Wars) VFW and distributed study brochures to Veterans. On September 26, 2013, recruitment efforts included a table set up and information distribution at the Zarrow Mental Health Symposium. September 26-30, 2013, recruitment-oriented staff tended a table at the Tulsa State Fair. Primary recruitment activities involved welcoming attendees and discussing the current research project as well as providing information materials to potential participants.

List of Activities:

- April 11 – Community Service Council Veterans Initiative monthly meeting
- April 12 – Mental Health Association "Crisis: Opportunity for Change" event
- April 18 – Tulsa Police Department presentation
- April 18 – Legal Aid Services of Oklahoma presentation
- April 22 – KWGS Public Radio Tulsa interview
- May 1 – Brookhaven Psychiatric Hospital monthly meeting
- May 7 – Human Skills and Resources (clinical services organization) presentation
- May 9 – Community Service Council Veterans Initiative monthly meeting
- May 21 – Laureate Psychiatric Clinic and Hospital LPCH luncheons for physicians/psychiatrists
- June 5 – Brookhaven Psychiatric Hospital monthly meeting
- June 6 – 30 Day Yellow Ribbon Event
- June 7 – Tulsa Tough athletic event
- June 13 – Community Service Council Veterans Initiative monthly meeting
- July 13–14 – 60 Day Yellow Ribbon Event
- July 14 – Brookhaven Psychiatric Hospital monthly meeting
- July 21 – Muskogee (Veterans Administration) VA Welcome Home event
- July 25 – Community Service Council Veterans Initiative monthly meeting
- August 16 – Brookhaven Psychiatric Hospital monthly meeting
- August 16 – Community Service Council Veterans Initiative monthly meeting
- August 22 – KOTV News on 6 interview
- August 27 – Presentation to Attorney General
- September 4 – Brookhaven Psychiatric Hospital monthly meeting
- September 5 – "Soul Wounds" veterans event at All Souls Unitarian Church

- September 12 – Community Service Council Veterans Initiative monthly meeting
- September 19 – Veteran Advisory Council monthly meeting
- September 20 – University of Tulsa Student Veteran Association presentation
- September 26 – Veterans of Foreign Wars) VFW presentation
- September 26 – Zarrow Mental Health Symposium
- September 26–30 – Tulsa State Fair

In the last year we have received 61 calls regarding the study, and 53 of the callers completed phone screening. Sixteen veterans were enrolled in the study. Ten of those veterans completed at least one fMRI scan. Six completed at least one session of the fMRI neurofeedback session. Three of those six have now completed the study. There are currently 5 veterans actively enrolled in the study and one who has completed screening assessments, but has not yet been officially enrolled in the study.

4. **KEY RESEARCH ACCOMPLISHMENTS:** Bulleted list of key research accomplishments emanating from this research. Project milestones, such as simply completing proposed experiments, are not acceptable as key research accomplishments. Key research accomplishments are those that have contributed to the major goals and objectives and that have potential impact on the research field.

Due to study preparation, securing human research approvals and initial data collection phase there is nothing to report for the period covered by this report.

5. **CONCLUSION:** Summarize the importance and/or implications with respect to medical and /or military significance of the completed research including distinctive contributions, innovations, or changes in practice or behavior that has come about as a result of the project. A brief description of future plans to accomplish the goals and objectives shall also be included.

Our efforts during year 1 have resulted in substantial progress toward accomplishing our aims for this project. We have secured all necessary approvals for administering the study protocol, and in addition we have secured a Certificate of Confidentiality. Concurrently, we have finalized all necessary methodological aspects of the study, including training in structured clinical interviewing as well as completion of the automated and individualized protocols (and related staff training) necessary for measuring emotional reactivity both inside and outside of the scanner environment. Multiple subjects have now completed this protocol, demonstrating its feasibility. Alongside the successful administration of our highly novel protocol to multiple subjects, we have made substantial progress in the development of the hardware and software systems for a stand-alone EEG system for neurofeedback as targeted in Aim 2 of the project. Given that we planned to test this EEG system during Year 2 of the project, we have made satisfactory progress in this domain as well. We also have developed a novel analytic method that will significantly reduce data loss due to subject motion. Finally, our increasingly robust recruitment campaign is now yielding a subject enrollment rate that we anticipate will be sufficient for allowing us to accomplish our aims for years 2 and 3 of this project. Collectively, we anticipate that these accomplishments in Year 1 of the project have situated our successfully collaborating team for further satisfactory progress throughout the remainder of the project period. As such, we remain well-positioned to develop and initially test a novel intervention that has the potential to advance both understanding of PTSD and our ability to successfully treat this chronic and costly condition.

6. PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:

a. List all manuscripts submitted for publication during the period covered by this report resulting from this project. Include those in the categories of lay press, peer-reviewed scientific journals, invited articles, and abstracts. Each entry shall include the author(s), article title, journal name, book title, editors(s), publisher, volume number, page number(s), date, DOI, PMID, and/or ISBN.

(1) Lay Press:
(2) Peer-Reviewed Scientific Journals:
(3) Invited Articles:
(4) Abstracts:

b. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.

Nothing to report.

7. **INVENTIONS, PATENTS AND LICENSES:** List all inventions made and patents and licenses applied for and/or issued. Each entry shall include the inventor(s), invention title, patent application number, filing date, patent number if issued, patent issued date, national, or international.

Nothing to report.

8. **REPORTABLE OUTCOMES:** Provide a list of reportable outcomes that have resulted from this research. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. This list may include development of prototypes, computer programs and/or software (such as databases and animal models, etc.) or similar products that may be commercialized.

1) We anticipated in the design of the PTSD study, given the larger problem with rapid head movements in clinical populations (PTSD, MDD and other psychiatric disorders) during fMRI and fMRI&EEG experiments, that advanced methods for motion correction would improve our capacity to address the main aims of our project. Therefore we developed a novel method for retrospective motion correction of fMRI data in simultaneous EEG-fMRI that employs the EEG array as a sensitive motion detector [17]. EEG motion artifacts are used to generate motion regressors describing rotational head movements with millisecond temporal resolution. These regressors are utilized for slice-specific motion correction of unprocessed fMRI data. The proposed EEG-assisted method of retrospective fMRI motion correction will be applied to improve quality of fMRI neurofeedback data for this study. It can reduce spurious correlations between the EEG and fMRI data caused by large and rapid head movements and greatly improve data quality, and reduce the number of subjects excluded from analysis due to motion artifacts. We are now actively working on a more practical and robust implementation and will utilize this novel technique on all already acquired fMRI and EEG data from veterans with combat-related PTSD.

2) We have begun EEG software development at the LIBR during month 12 of the project for the purpose of project Aim #2: development of stand-alone real-time EEG neurofeedback system.

9. **OTHER ACHIEVEMENTS:** This list may include degrees obtained that are supported by this award, development of cell lines, tissue or serum repositories, funding applied for based on work supported by this award, and employment or research opportunities applied for and/or received based on experience/training supported by this award.

   Nothing to report.

10. REFERENCES: List all references pertinent to the report using a standard journal format (i.e., format used in *Science*, *Military Medicine*, etc.).

1. Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (American Psychiatric Association, 2000).
2. Milliken, C. S., Auchterlonie, J. L. & Hoge, C. W. Longitudinal assessment of mental health problems among active and reserve component soldiers returning from the Iraq war. Jama 298, 2141-8, (2007).
3. Kessler, R. C. Posttraumatic stress disorder: the burden to the individual and to society. J Clin Psychiatry 61 Suppl 5, 4-12; discussion 13-4, (2000).
4. Rauch, S. L., Shin, L. M. & Phelps, E. A. Neurocircuitry models of posttraumatic stress disorder and extinction: human neuroimaging research--past, present, and future. Biol Psychiatry 60, 376-82 (2006).
5. Shin, L. M., Rauch, S. L. & Pitman, R. K. Amygdala, medial prefrontal cortex, and hippocampal function in PTSD. Ann N Y Acad Sci 1071, 67-79, (2006).
6. Protopopescu, X. et al. Differential time courses and specificity of amygdala activity in posttraumatic stress disorder subjects and normal control subjects. Biol Psychiatry 57, 464-73 (2005).
7. Rauch, S. L. et al. Exaggerated amygdala response to masked facial stimuli in posttraumatic stress disorder: a functional MRI study. Biol Psychiatry 47, 769-76, (2000).
8. Sergerie K, Chochol C, Armony JL. The role of the amygdala in emotional processing: a quantitative meta-analysis of functional neuroimaging studies. Neurosci Biobehav Rev. 32(4):811-30, (2008).
9. Shin, L. M. et al. A functional magnetic resonance imaging study of amygdala and medial prefrontal cortex responses to overtly presented fearful faces in posttraumatic stress disorder. Arch Gen Psychiatry 62, 273-81, (2005).
10. deCharms, R. C. Applications of real-time fMRI. Nat Rev Neurosci 9, 720-729, (2008).
11. Zotev, V., Krueger, F., Phillips, R., Alvarez, R. P., Simmons, W. K., Bellgowan, P., Drevets, W. C., Bodurka, J. Self-regulation of amygdala activation using real-time fMRI neurofeedback. PLoS ONE 6(9), e24522, (2011).

12. Mulert, C., Lemieux, L. (Eds) EEG-FMRI: Physiological basis, Technique and Applications. Springer (2010).
13. Allen, J.J.B., Harmon-Jones, E., Cavender, J.H., Manipulation of frontal EEG asymmetry through biofeedback alters self-reported emotional responses and facial EMG. Psychophysiology 38, 685–693, (2001).
14. Gordon, E., Palmer, D.M., Cooper, N., EEG alpha assymetry in schizophrenia, depression, PTSD, panic disorders, ADHD and conduct disorder. Clinical EEG and Neuroscience 41, 178-183, (2010).
15. Harmon-Jones, E, Gable, P.A., Peterson, C. K. The role of asymmetric frontal cortical activity in emotion-related phenomena: a review and update. Biol. Psychol 84(3), 451-462, (2010).
16. Yuan, H., Zotev, V., Phillips, R., Drevets, W.C., Bodurka, J. Spatiotemporal dynamics of the brain at rest – exploring EEG microstates as electrophysiological signatures of BOLD resting state networks. Neuroimage 60(4), 2062-2072, (2012).
17. Zotev, V., Yuan, H., Phillips, R., Bodurka, J. EEG-assisted retrospective motion correction for fMRI: E-REMCOR. Neuroimage 63, 698-712, (2012).

11. **APPENDICES:** Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

NOTE:

TRAINING OR FELLOWSHIP AWARDS: For training or fellowship awards, in addition to the elements outlined above, include a brief description of opportunities for training and professional development. Training activities may include, for example, courses or one-on-one work with a mentor. Professional development activities may include workshops, conferences, seminars, and study groups.

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on this eReceipt System https://cdmrp.org/Program_Announcements_and_Forms/ and under "Forms" on https://www.usamraa.army.mil) should be updated and submitted with attachments.

MARKING OF PROPRIETARY INFORMATION: Data that was developed partially or exclusively at private expense shall be marked as "Proprietary Data" and Distribution Statement B included on the cover page of the report. Federal government approval is required before including Distribution Statement B. The recipient/PI shall coordinate with the GOR to obtain approval. REPORTS NOT PROPERLY MARKED FOR LIMITATION WILL BE DISTRIBUTED AS APPROVED FOR PUBLIC RELEASE. It is the responsibility of the Principal Investigator to advise the GOR when restricted limitation assigned to a document can be downgraded to "Approved for Public Release." DO NOT USE THE WORD "CONFIDENTIAL" WHEN MARKING DOCUMENTS. See term entitled "Intangible Property – Data and Software Requirements" and https://mrmc.amedd.army.mil/index.cfm?pageid=researcher_resources.technical_reporting for additional information.